AMENDMENTS TO CLAIMS

Claim 1. (Currently Amended) A compound which has the structure

$$\begin{array}{c|c}
R^{2a} & R^{2b} \\
R^{2a} & X_2 \\
R^{2c} & X_4 \\
R^{1} & R^{1}
\end{array}$$

$$\begin{array}{c|c}
R^2 & R^3 \\
R & (CH_2)_m \\
R & (CH_2)_m
\end{array}$$

wherein m is 0, 1 or 2; n is 0, 1 or 2;

Q is C or N;

A is $(CH_2)_x$ where x is 1 to 5 or A is $(CH_2)_x^1$ where x^1 is 1 to 5 with an alkenyl bond or an alkynyl bond embedded anywhere in the chain, or A is $-(CH_2)_x^2$ -O- $-(CH_2)_x^3$ - where x^2 is 0 to 5 and x^3 is 0 to 5, provided that at least one of x^2 and x^3 is other than 0;

B is a bond or is $(CH_2)_x$ where x^4 is 1 to 5;

X is CH or N;

 X_2 is C, N, O or S;

 X_3 is C, N, O or S;

 X_4 is C, N, O or S;

 X_5 is C, N, O or S;

X₆ is C, N, O or S;

provided that at least one of X2, X3, X4 X5 and X6 is N; and at least one of X2, X3, X4 X5 and X6 is C,

R¹ is H or alkyl;

R² is H, alkyl, alkoxy, halogen, amino or substituted amino or cyano;

R^{2a}, R^{2b} and R^{2c} may be the same or different and are selected from H, alkyl, alkoxy, halogen, amino or substituted amino or cyano;

R³ is selected from H, alkyl, arylalkyl, aryloxycarbonyl, alkyloxycarbonyl, alkynyloxycarbonyl, alkynyloxycarbonyl, alkyloxycarbonyl, aryloxycarbonyl, cycloheteroalkyl, heteroarylcarbonyl, heteroaryl-heteroarylalkyl, alkylcarbonylamino, aryloxycarbonylamino, heteroarylcarbonylamino, aryloxycarbonylamino, heteroarylcarbonyl, alkylsulfonyl, alkenylsulfonyl, heteroaryloxycarbonyl, cycloheteroalkyloxycarbonyl, heteroarylalkyl, aminocarbonyl, substituted

aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, heteroarylalkenyl, cycloheteroalkylheteroarylalkyl; hydroxyalkyl, alkoxy, alkoxyaryloxycarbonyl, arylalkyloxycarbonyl, alkylaryloxycarbonyl, arylalkylarylalkyl, aryloxyarylalkyl, haloalkoxyaryloxycarbonyl, alkoxycarbonylaryloxycarbonyl, aryloxyaryloxycarbonyl, arylalkenyloxycarbonyl, arylalkenyloxycarbonyl, arylalkenyloxycarbonyl, arylalkylcarbonyl, arylalkylcarbonyl, arylalkylcarbonyl, arylalkyloxycarbonyl, arylalkylsulfonyl, arylalkylcarbonyl, arylalkylcarbonyl, arylalkylsulfonyl, arylalkylsulfonyl, arylalkylsulfonyl, arylalkoxycarbonyl, arylalkylsulfonyl, heteroarylalkyl, alkoxyarylcarbonyl, aryloxyheteroarylalkyl, heteroarylalkyl, arylalkenylarylalkyl, arylalkoxyarylalkyl, arylalkenylheteroarylalkyl, arylaminoarylalkyl, aminocarbonylarylalkyl;

Y is CO_2R^4 where R^4 is H or alkyl, or a prodrug ester, or Y is a C-linked 1-tetrazole, a phosphinic acid of the structure $P(O)(OR^{4a})R^5$ where R^{4a} is H or a prodrug ester, R^5 is alkyl or aryl, or a phosphonic acid of the structure $P(O)(OR^{4a})_2$;

 $(CH_2)_x$, $(CH_2)_x^1$, $(CH_2)_x^2$, $(CH_2)_x^3$, $(CH_2)_x^4$, $(CH_2)_m$, and $(CH_2)_n$ may be optionally substituted with 1, 2 or 3 substituents <u>selected from alkyl, alkenyl, halogen, cyano, hydroxy, alkoxy, amino,</u> thioalkyl, keto, C_3 - C_6 cycloalkyl, alkylcarbonylamino or alkylcarbonyloxy;

and wherein the term "heteroaryl" alone or as part of another group refers to a 5- or 6-membered aromatic ring which includes 1, 2, 3 or 4 heteroatoms which is nitrogen, oxygen or sulfur, and such rings optionally fused to an aryl, cycloalkyl, heteroaryl or cycloheteroalkyl ring;

the term "cycloheteroalkyl" alone or as part of another group refers to a 5-, 6- or 7-membered saturated or partially saturated ring which includes 1 to 2 heteroatoms which is nitrogen, oxygen or sulfur, and such rings optionally fused to a cycloalkyl, aryl, heteroaryl or cycloheteroalkyl ring;

including and all stereoisomers thereof, <u>a</u> prodrug esters <u>ester</u> thereof, <u>and or a</u> pharmaceutically acceptable <u>salts</u> thereof,

and specifically excluding the structure as shown below:

$$\begin{array}{c|c}
R^{2a} & R^{2b} \\
R^{2a} & R^{2a} \\
R^{2c} & X_3 \\
R^{2} & R^{2} \\
X_4 & R^{1}
\end{array}$$

$$\begin{array}{c|c}
R^2 & R^3 \\
(CH_2)_m & N \\
(CH_2)_m & N
\end{array}$$

$$\begin{array}{c|c}
(CH_2)_m & N
\end{array}$$

where $X_2 = N$, $X_3 = C$, $X_4 = O$ or S, Z = O or a bond.

Claim 2. (Cancelled).

Claim 3. (Original) The compound as defined in Claim 1 wherein A is $-(CH_2)x^2$ -O-.

Claim 4. (Cancelled).

Claim 5. (Original) The compound as defined in Claim 1 wherein B is a bond.

Claim 6. (Currently Amended) The compound as defined in Claim 1 wherein

$$\frac{\mathcal{Z}_{X_3}}{X_4-X_5} \xrightarrow{X_2} \frac{\mathcal{X}_2}{X_4+X_5} \xrightarrow{X_5} \frac{\mathcal{X}_2}{X_4+X_5} \xrightarrow{X_5} \frac{\mathcal{X}_2}{X_5} \xrightarrow{X_5} \frac{\mathcal{X}_3}{X_4+X_5} \xrightarrow{X_5} \frac{\mathcal{X}_4}{X_5} \xrightarrow{X_5} \frac{\mathcal{X}_5}{X_5} \xrightarrow{X_5}$$

Claim 7. (Original) The compound as defined in Claim 1 wherein R³ is arylalkyloxycarbonyl, arylheteroarylalkyl, aryloxyarylalkyl, aryloxycarbonyl, haloaryl-oxycarbonyl, alkoxyaryloxycarbonyl, alkylaryloxycarbonyl, aryloxyaryloxycarbonyl, heteroaryloxycarbonyl, aryloxyarylcarbonyl, arylalkenyloxycarbonyl, cycloalkylaryloxycarbonyl, arylalkylarylcarbonyl, heteroaryl-heteroarylalkyl, cycloalkyloxyaryloxycarbonyl, heteroaryl-heteroarylalkyl, cycloalkyloxyaryloxycarbonyl, heteroaryl-heteroarylcarbonyl, arylalkylsulfonyl, arylalkenylsulfonyl, alkoxyarylalkyl, arylthiocarbonyl, cycloheteroalkyloxycarbonyl, or polyhaloalkylaryloxy-carbonyl, which may be optionally substituted.

Claim 8. (Currently Amended) The compound as defined in Claim 1 which has the structure

Claim 9. (Currently Amended) The compound as defined in Claim 1 which has the structure

$$R^{2a}$$
 X_{2}
 X_{4}
 X_{5}
 R^{1}
 $(CH_{2})_{m}$
 $(CH_{2})_{m}$
 $(CH_{2})_{m}$
 $(CH_{2})_{m}$

Claim 10. (Original) The compound as defined in Claim 9 wherein R^{2a} , R^{2b} and R^{2c} are each H; R^1 is alkyl, x^2 is 1 to 3; R^2 is H; m is 0 or $(CH_2)_m$ is CH_2 or CHOH or CH-alkyl, X is C, X_2 , X_3 , X_4 , X_5 and X_6 represent a total of 1, 2 or 3 nitrogens, $(CH_2)_n$ is a bond or CH_2 and R^3 is alkoxyaryloxycarbonyl.

Claim 11. (Original) The compound as defined in Claim 10 wherein R¹ is CH₃ and R³ is methyloxyphenyloxycarbonyl.

Claim 12. (Currently Amended) The compound as defined in Claim 1 wherein

$$\begin{array}{c}
X_{2} \\
X_{3} \\
X_{4} \\
X_{5}
\end{array}$$
is
$$\begin{array}{c}
N \\
N
\end{array}$$

$$\begin{array}{c}
N \\
N
\end{array}$$
and
$$\begin{array}{c}
N \\
N
\end{array}$$

Claim 13. (Currently Amended) The compounds as defined in Claim 1 having the structure

Claim 14. (Original) A pharmaceutical composition comprising a compound as defined in Claim 1 and a pharmaceutically acceptable carrier therefor.

Claim 15. (Currently Amended) A method for treating diabetes, Type 2 diabetes, and related diseases such as insulin resistance, hyperglycemia, hyperinsulinemia, elevated blood levels

of fatty acids or glycerol, hyperlipidemia, obesity, hypertriglyceridemia, inflammation, Syndrome X, diabetic complications, dysmetabolic syndrome, <u>and</u> atherosclerosis, and related diseases, which comprises <u>administgering administering</u> to a patient in need of treatment a therapeutically effective amount of a compound as defined in Claim 1.

Claim 16. (Currently Amended) A method for treating early malignant lesions, ductal carcinoma in situ of the breast, lobular carcinoma in situ of the breast, premalignant lesions, fibroadenoma of the breast, prostatic intraepithelial neoplasia (PIN), liposarcomas and various ether epithelial tumors which are (including breast, prostate, colon, ovarian, gastric and or lung[[)]] tumors, irritable bowel syndrome, Crohn's disease, gastric ulceritis, and osteoporosis and proliferative diseases and such as psoriasis, which comprises administering to a patient in need of treatment a therapeutically effective amount of a compound as defined in Claim 1.

Claim 17. (Original) A pharmaceutical combination comprising a compound as defined in Claim 1 and a lipid-lowering agent, a lipid modulating agent, an antidiabetic agent, an anti-obesity agent, an antihypertensive agent, a platelet aggregation inhibitor, and/or an antiosteoporosis agent.

Claim 18. (Original) The combination as defined in Claim 17 wherein the antidiabetic agent is 1, 2, 3 or more of a biguanide, a sulfonyl urea, a glucosidase inhibitor, a PPAR γ agonist, a PPAR α/γ dual agonist, an SGLT2 inhibitor, a DP4 inhibitor, an aP2 inhibitor, an insulin sensitizer, a glucagon-like peptide-I (GLP-I), insulin and/or a meglitinide, the anti-obesity agent is a beta 3 adrenergic agonist, a lipase inhibitor, a serotonin (and dopamine) reuptake inhibitor, a thyroid receptor agonist, an aP2 inhibitor, a cannabinoid receptor-1 antagonist and/or an anorectic agent, the lipid lowering agent is an MTP inhibitor, an HMG CoA reductase inhibitor, a squalene synthetase inhibitor, a fibric acid derivative, an upregulator of LDL receptor activity, a lipoxygenase inhibitor, a farnesoid receptor (FXR) agonist, a liver X receptor (LXR) agonist, a CETP inhibitor or an ACAT inhibitor, the antihypertensive agent is an ACE inhibitor, angiotensin II receptor antagonist, NEP/ACE inhibitor, calcium channel blocker and/or β -adrenergic blocker.

Claim 19. (Original) The combination as defined in Claim 18 wherein the antidiabetic agent is 1, 2, 3 or more of metformin, glyburide, glimepiride, glipyride, glipizide, chlorpropamide, gliclazide, acarbose, miglitol, pioglitazone, rosiglitazone, balaglitazone, insulin, Gl-262570, isaglitazone, JTT-501, NN-2344, L895645, YM-440, R-119702, AJ9677, repaglinide, nateglinide,

KAD1129, AR-HO39242, GW-409544, KRP297, AZ-242, AC2993, LY315902, P32/98 and/or NVP-DPP-728A, the anti-obesity agent is orlistat, ATL-962, AJ9677, L750355, CP331648, sibutramine, topiramate, axokine, dexamphetamine, phentermine, phenylpropanolamine, rimonabant (SR-141716) and/or mazindol, the lipid lowering agent is pravastatin, lovastatin, simvastatin, atorvastatin, fluvastatin, itavastatin, visastatin, rosuvastatin, pitavastatin, fenofibrate, gemfibrozil, clofibrate, avasimibe, ezetimibe, TS-962, MD-700, cholestagel, niacin and/or LY295427, the antihypertensive agent is an ACE inhibitor which is captopril, fosinopril, enalapril, lisinopril, quinapril, benazepril, fentiapril, ramipril or moexipril; an NEP/ACE inhibitor which is omapatrilat, [S[(R*,R*)]-hexahydro-6-[(2-mercapto-1-oxo-3-phenylpropyl)amino]-2,2-dimethyl-7-oxo-1H-azepine-1-acetic acid (gemopatrilat) or CGS 30440;

an angiotensin II receptor antagonist which is irbesartan, losartan, telmisartan or valsartan; amlodipine besylate, prazosin HCI, verapamil, nifedipine, nadolol, propranolol, carvedilol, or clonidine HCI, the platelet aggregation inhibitor is aspirin, clopidogrel, ticlopidine, dipyridamole or ifetroban.